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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	PAPER NUMBER
1643	

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11/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,168	ARAP ET AL.	
	Examiner	Art Unit	
	Meera Natarajan	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11-22 and 55-61* is/are pending in the application.

4a) Of the above claim(s) *2,15,20-22 and 57-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 11-14, 16-19, 55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/23/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). Applicant has inadvertently left out Claim 12. The Claims have been renumbered accordingly. Misnumbered claims 13-62 have now been renumbered as claims 12-61.

Election/Restrictions

2. Applicant's election without traverse of Group I, claims 1, 3, 4, 11-21, 55 and 56, in the reply filed on 09/20/2007 is acknowledged.

3. Applicant has cancelled claims 4-10 and 23-54 and added claims 57-61. Claims 57-61 depend from Group I and will be examined accordingly.

4. Claims 2, 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/20/2007.

5. Claim 15, 20, 21, 57-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/20/2007.

6. After further consideration the species requirement for "targeting peptide" SEQ ID NO. has been extended to include SEQ ID NOs: 5-33 and 109.

7. Claims 1, 3, 11-14, 16-19, 55 and 56 will be examined on the merits.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 11, 14, 55, and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 11 recites "detecting prostate cancer cells in said sample cancer in bone marrow". It is unclear what applicant means by "said sample cancer in bone marrow". Does applicant mean detecting prostate cancer cells in a sample of bone marrow tissue from a patient? Clarification is required. For examination purposes, Claim 11 will be examined as "The method of claim 1, further comprising detecting prostate cancer cells in said sample."

11. Claim 14 recites "the method of claim 4", however claim 4 has been cancelled. Therefore Claim 14 is indefinite because it depends from limitations that have been cancelled. Correction is required. For examination purposes, Claim 14 will be examined as depending from Claim 1.

12. Claim 55 recites "the method of claim 6", however claim 6 has been cancelled. Therefore Claim 55 and dependent claim 56 are indefinite because it depends from

limitations that have been cancelled. Correction is required. For examination purposes, Claim 55 will be examined as depending from Claim 1.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a targeting peptide that targets prostate cancer tissue that comprises *at least* three contiguous amino acids of SEQ ID NOs: 5-35, 37, 83-129. The claims are broadly drawn to ***any*** peptide that comprises at least three contiguous amino acids of the sequences claimed.

15. The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli

> Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

16. The genus being claimed in the current application is a "targeting peptide that selectively binds to prostate cancer tissue". The disclosure defines a "targeting peptide that selectively binds to prostate cancer tissue" as ***any*** peptide that comprises at least three contiguous amino acids of SEQ ID NOs: 5-35, 37, 83-129. The applicant provides no identifying characteristics other than a structural limitation. The application does not disclose any other structural or physical properties that correlate to the functional aspect of being a "targeting peptide that selectively binds to prostate cancer tissue". There are no chemical properties to confer the desired function disclosed in the current application to define a "targeting peptide". The specification teaches only peptides comprising amino acids AGG can selectively target prostate cancer tissue. This one example does not support the broad scope of the claims. Based on the lack of the identification of any characteristics other than the structural limitation, the application provides insufficient descriptive support to demonstrate possession of the claimed genus.

17. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for targeting peptides that target prostate cancer tissue that comprise at least the amino acids AGG (SEQ ID NO:5-35 and 37), does not reasonably provide enablement for any targeting peptide that comprises at least *any* three contiguous amino acids of SEQ ID NOs: 83-129. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

18. The Claim is broadly drawn to a targeting peptide comprising at least *any* three contiguous amino acids of a sequence selected from *any* of SEQ ID NO: 5-35, 37, and 83-129.

19. It is known in the art that some tripeptides are capable of binding to their receptors. Ruoslahti et al. teach integrin-binding activity of adhesion proteins can be reproduced by short synthetic peptides containing the RGD sequence (see Abstract). Such peptides promote cell adhesion when insolubilized onto a surface, and inhibit it when presenting to cells in solution. Reagents that bind selectively to only one or a few of the RGD-directed integrins can be designed by cyclizing peptides with selected sequences around the RGD and by synthesizing RGD mimics (see Abstract). Applicant's broad scope of the claim drawn to ***any*** three contiguous amino acids from the claimed SEQ ID NOs would incorporate a large number of tripeptides that are not known in the art. The specification only provides evidence for peptides that selectively bind to prostate cancer tissue comprising the 3 amino acids AGG (see specification Example 2). The specification does not provide any evidence that targeting peptides

comprising *any* selection of 3 contiguous amino acids from SEQ ID NO: 83-129 would be enabled for selectively binding to prostate cancer tissue. Applicant discloses in the specification on p. 121 that SEQ ID NOs: 83-129 contain no obvious homologies nor do they contain the targeting motif AGG. Example 2 indicates the motif AGG was found only in prostate cancer tissue, whereas other tripeptide motifs screened were all found in atleast one other tissue (see p. 67 1st paragraph). The instant application has not shown that just any three contiguous amino acids of SEQ ID NO: 5-35, 37, and 83-129 can bind except for peptides containing the amino acids AGG.

Therefore one of ordinary skill in the art would have to perform undue experimentation in order to determine what 3 contiguous amino acids of SEQ ID NOs: 83-129 could selectively bind to prostate cancer tissue.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 1, 3, 11-14, 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Ellerby et al. (WO/2000/042973).

22. The claims are drawn to a method comprising obtaining an 100 amino acid or less peptide with a cancer targeting motif that selectively binds to prostate cancer tissue, attaching an therapeutic pro-apoptotic agent, (KLAKLAK)2, to form a complex

and exposing said complex to a sample of prostate tissue and diagnosing prostate cancer.

23. Ellerby et al. teach a prostate-homing pro-apoptotic peptide that contains a prostate-homing peptide linked to an antimicrobial peptide. The prostate-homing peptide portion comprises the sequence SMSIARL or a functionally equivalent sequence, and the antimicrobial peptide portion comprises the sequence (KLAKLAK)2 (see p. 6). Sequence SMSIARL has 3 contiguous amino acids to SEQ ID NO: 109 of the instant application. Ellerby et al. further teach antibody staining of tissue sections showed that the SMSIARL peptide localized to prostate tissue, but not to other tissues after an intravenous injection of the peptide into mice. Control peptides also did not accumulate in the prostate (see Figure 6 description p. 100-102). The reference teaches each and every limitation of the claims.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

26. Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellerby et al. in view of Campbell et al. (American J. of Pathol. Vol. 158, pp.25-32, 2001) and Schally et al. (The Prostate Vol. 45, pp.158-166, 2000).

11. The claims are drawn to a method comprising obtaining an 100 amino acid or less peptide with a cancer targeting motif that selectively binds to prostate cancer tissue, attaching an therapeutic pro-apoptotic agent, (KLAKLAK)2, to form a complex and exposing said complex to a sample of prostate tissue and diagnosing prostate cancer. The method is also drawn to further comprising categorizing a prostate cancer as androgen-dependent or androgen-independent and expression of IL-11R alpha in the blood vessels of said prostate cancer.

27. The teachings of Ellerby et al. are presented in the 102(b) rejection set forth above. Ellerby et. al. does not teach categorizing prostate cancer as androgen-dependent or androgen-independent and expression of IL-11R alpha in the blood vessels of said prostate cancer.

28. Campbell et al. teach increased expression of interleukin-11 receptor alpha in prostate carcinoma (see abstract).

29. Schally et al. teach the use of peptide analogs in the therapy of prostate androgen-dependent or androgen-independent cancer (see abstract).

30. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to perform the method of Claim 1 with prostate

cancer cells that have been categorized as androgen-independent or androgen-dependent and express IL-11R alpha in their blood vessels. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Ellerby et al., Campbell et al., and Schally et al. because Campbell et al. teach that IL-11R alpha is overexpressed in prostate carcinoma and Schally et al. teach that the use of peptide analogs for treatment of androgen-dependent and androgen-independent prostate cancer have been effective.

Conclusion

31. Claims 1, 3, 11-14, 16-19, 55 and 56 are rejected.

32. No claim is allowed.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meera Natarajan whose telephone number is 571-270-3058. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

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